Regenerative Capacity of Old Muscle Stem Cells Declines without Significant Accumulation of DNA Damage.

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Authors: Wendy Cousin, Michelle Liane Ho, Rajiv Desai, Andrea Tham, Robert Yuzen Chen, Sunny Kung, Christian Elabd, Irina M Conboy

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Public Summary:
If the regenerative / proliferative potential of the aged tissue stem cells is boosted they will make healthy organs without genomic instability, because there is no accumulation of DNA damage in stem cells with age and DNA repair remains effective in the old tissue stem cells.

Scientific Abstract:
The performance of adult stem cells is crucial for tissue homeostasis but their regenerative capacity declines with age, leading to failure of multiple organs. In skeletal muscle this failure is manifested by the loss of functional tissue, the accumulation of fibrosis, and reduced satellite cell-mediated myogenesis in response to injury. While recent studies have shown that changes in the composition of the satellite cell niche are at least in part responsible for the impaired function observed with aging, little is known about the effects of aging on the intrinsic properties of satellite cells. For instance, their ability to repair DNA damage and the effects of a potential accumulation of DNA double strand breaks (DSBs) on their regenerative performance remain unclear. This work demonstrates that old muscle stem cells display no significant accumulation of DNA DSBs when compared to those of young, as assayed after cell isolation and in tissue sections, either in uninjured muscle or at multiple time points after injury. Additionally, there is no significant difference in the expression of DNA DSB repair proteins or globally assayed DNA damage response genes, suggesting that not only DNA DSBs, but also other types of DNA damage, do not significantly mark aged muscle stem cells. Satellite cells from DNA DSB-repair-deficient SCID mice do have an unsurprisingly higher level of innate DNA DSBs and a weakened recovery from gamma-radiation-induced DNA damage. Interestingly, they are as myogenic in vitro and in vivo as satellite cells from young wild type mice, suggesting that the inefficiency in DNA DSB repair does not directly correlate with the ability to regenerate muscle after injury. Overall, our findings suggest that a DNA DSB-repair deficiency is unlikely to be a key factor in the decline in muscle regeneration observed upon aging.

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